

of the importance of abdominal adhesions, and our progress in their diagnosis is especially by means of the roentgen-ray. A less pleasing subject for our contemplation is our inability effectually to deal with such adhesions when they do exist and cause symptoms.

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### THE TREATMENT OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM WITH INTRASPINAL INJECTIONS OF MERCURIALIZED SERUM.

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UNTIL recently the treatment of syphilis of the central nervous system was not essentially different from that of syphilis elsewhere in the body. Because of this, results in these cases have been far from satisfactory.

Since the discovery that the *Spirocheta pallida* are the active agents and are found viable in the tissues and exudates in the so-called parasyphilitic diseases, the tendency has been to consider these cases merely cerebrospinal syphilis and to lose sight of the finer anatomical localizations. This also is in part due to the rapid advance in our laboratory methods.

Ravaut was the first to call attention to the diagnostic importance of a meningeal reaction in the very earliest stages of syphilis, which was too slight to be detected in any other way, except by the examination of the cerebrospinal fluid. Udo Wile, in this country, has been very active in substantiating this work of Ravaut's. This can mean only one thing—that the central nervous system is involved in the early stages in the majority of cases. Systemic treatment here is usually quite efficacious, even though there may

be an extensive meningitis, with headache and other functional disturbance.

Later, however, the changes in the central nervous system and its envelopes are more chronic and yield less readily to medication.

In the different anatomical types of nerve syphilis, such as the interstitial, the parenchymatous, and the essentially vascular, treatment will or will not yield results, depending on the accessibility of the diseased region to the medication. In the interstitial type, which includes meningitis luetica, meningo-arteritis, and gummata, the results from systemic treatment have been good, because symptoms arising therefrom have been functional and depend on the amount of exudate and pressure, the resolution of which often yields brilliant functional results. When, however, the nerve tracts or centers have been destroyed, full restoration of function cannot be expected.

In the parenchymatous type, which includes the so-called parasyphilitic diseases, irritation and destruction of nervous elements seem to be the essential features. Here, results of systemic treatment have been somewhat disappointing, except when the irritative symptoms have been due to active inflammatory processes.

The seat of the active lesion in most cases of tabes, namely, radiculitis, probably explains why some cases yield to the treatment better than those of general paresis, in which the spirochete and round-cell infiltration are scattered throughout the cerebral cortex.

Swift says of this: "The separateness of the dorsal roots may result in greater accessibility to the remedial agent, and it is conceivable that if all the radicular nerves and dorsal ganglia were gathered in one area, as in the cerebral cortex, the arrest of tabes might be as unsatisfactory as is the treatment of paresis."

Before the advent of salvarsan, treatment of nerve syphilis with mercury was far from encouraging because there were so many relapses. The present drift of opinion is that in the exudative, inflammatory, gummatous, and arterial forms, salvarsan is by far the most efficient remedy we possess. Schaller, as early as 1912, states in his conclusions that "the relief obtained from one intravenous injection of salvarsan appears to be temporary in the majority of cases."

Since large and more frequent doses have been given there are fewer neurorecidives and fewer relapses.

The use of salvarsan, which at first promised to yield such brilliant results, has in many cases, even with prolonged treatment, not given the expected results.

Just why was this? One or two answers suggest themselves—either irreparable changes had taken place in the nervous system or the drug failed to reach the seat of infection. Careful chemical investigations of the cerebrospinal fluids have shown no trace of

arsenic after the intravenous administration of neosalvarsan, and only very slight traces after salvarsan.

Swift and Ellis, in this country, conceived the brilliant idea that the administration of a salvarsanized serum into the sub-arachnoid space itself would possibly alter some of the local conditions which were evidently not reached by intravenous administration.

The results of their studies are manifold. Reports of patients who were quickly relieved began to appear. Some observers questioned the efficacy of the method, arguing that the cause of the improvement in clinical symptoms was the intravenous administration, and not its local application, and that the improvement in the cerebrospinal fluid findings was due to the withdrawal and subsequent dilution of the remaining fluid by the injected serum. Sachs, Strauss, and Kaliski have shown that up to forty-five minutes after the administration of 0.6 gm. salvarsan intravenously, only from 0.00004 to 0.0001 gm. of metallic arsenic could be detected in 20 c.c. whole blood; after forty-five minutes practically no free arsenic could be demonstrated.

Other workers, especially Marinesco and Ravaut, injected unchanged neosalvarsan in aqueous solution into the subdural space, but the reactions were severe and the results doubtful.

Great caution has to be exercised in the use of these unstable arsenical preparations, because of their irritative and toxic properties. This was shown in the very unfortunate circumstance which happened on our coast some months ago.

Ravaut, in 1913, had treated two cases of cerebrospinal syphilis with injections of mercurial salts into the subdural space, with marked improvement. Neither case had been followed more than a few weeks. Byrnes, in 1913, believed that many patients who were receiving the Swift-Ellis treatment were also being actively treated with mercury. In those patients who were receiving mercury, especially the inunctions, the presence of mercury (0.0000059 gm. per c.c.) could be demonstrated in the serum, an amount equal to the salvarsan content of salvarsanized serum, so that these patients were receiving a mercurialized as well as a salvarsanized serum.

Byrnes used, in general, the Swift-Ellis technic for the preparation and administration of the serum, except that no drug was administered before withdrawing the blood.

The preparation of patients and technic of administration of the serum in the cases reported below are essentially that of Byrnes' original procedure.

1. For one week the patient is given full doses of mercury, preferably 1 dram of the ointment inunctioned every night.

2. Forty c.c. blood are collected in dry sterile centrifuge tubes. The blood is centrifuged immediately and then placed in a

refrigerator for eighteen to twenty-four hours when it is again centrifuged for fifteen or twenty minutes and 18 to 20 c.c. serum are pipetted off.

3. One c.c. of a solution of mercuric chloride in distilled water, which contains  $\frac{1}{6}$  of a grain of bichloride, is added to the serum.

4. This prepared serum, which should be perfectly clear, is then heated at 56° C. (132° F.) for half an hour.

5. A lumbar puncture is performed. Spinal fluid is removed until the pressure reads about 30 mm.

6. The prepared serum is slowly administered by gravity, at body temperature.

7. The patient is placed in a bed, the foot of which is elevated eight inches, for four hours.

8. Liquid diet is ordered.

9. Morphin sulphate (gr.  $\frac{1}{4}$ ) is prescribed if necessary.

Difficulty in getting clear serum which contained no hemoglobin was encountered at first, but since all apparatus used is perfectly dry, there have been no severe reactions, which will be described in one or two of our earlier cases.

For determining the efficacy of this method I have determined to apply it for certain indications, only general paresis and in tabetics suffering from lancinating crises in the legs. Since gastric crises may be due to causes extra spinal, *i. e.*, disease of the sympathetic, it was decided not to treat tabetics with the latter manifestation as the only complaint by this method.

Twenty-five patients have been treated by this method in the last seven months—125 injections form the basis of this report. On an average, 5 injections were given each patient. One to two weeks' interval elapsed and all reaction had entirely subsided before a second injection was given in any case. A report of the more interesting cases follows. In all there were treated: Erb's syphilitic spastic spinal paralysis, 2 cases, 6 injections; general paresis, 3 cases, 15 injections; tabes dorsalis, 20 cases, 104 injections.

The luetin was done on patients having had no potassium iodid before or during the test. Detailed report of the most instructive cases follows.

CASE I.—Erb's syphilitic spastic spinal paralysis.

E. H., aged forty-one years; German. Entered the San Francisco Hospital September 24, 1914, complaining of inability to walk.

The patient had had gonorrhea in 1903 and a primary sore in 1908. The onset of his present trouble dated from 1912, with paresthesia of the buttocks, as if he were sitting on something cold. Pain in the left ankle soon followed. Six months later he suddenly lost the use of both legs. This lasted seven months, when slight power returned so that he could get around with the use of two canes. One year later a relapse occurred. During this time he was given five salvarsan injections and many mercurial rubs. No

marked improvement. Examination at this time showed a spastic paraplegia with marked weakness of the quadriceps extensor and the peroneals. The adductors were spastic.

Slight deafness in the left ear; pupils equal and react actively to light.

*Reflexes:* Knee-jerks, right and left, both exaggerated. Ankle-jerks exaggerated.

Babinski positive, right and left. Right superficial abdominals left.

Bathoesthesia of both big toes. No marked sensory involvement elsewhere.

Marked pains encircling lower abdomen were present. Much incontinence of urine, especially at night.

Mere. serum.	Date.	Cerebrospinal fluid.			Wassermann.			Reaction.	Remarks.
		Pressure.	Cells.	Albumin	Blood.	C. S. F.	Luetin.		
I	Mar. 27	280	200	+	—	—	+	To 104° vomit headache	Bloody serum.
II	May 19	?	80	Slight	—	—	—	None; temp. 102°	Better control of urination; pains disappeared.
III	June 17	130	38	—	—	—	—	No reaction; temp. 100°	Complete control of urine. No pains.

The reaction was very severe after the first treatment, due to contamination of the serum, with hemoglobin. This patient after the second injection had no further girdle sensations or pain in the legs. The bladder gave much less trouble. He, however, has no better use of his legs since the treatment.

#### CASE II.—*Tabes dorsalis.*

H. M., aged forty-nine years; electrician.

Entered the San Francisco Hospital July 1, 1915, complaining of general weakness and dizziness.

Gonorrhea and probable chancre thirty-three years ago. Some alcoholism. Onset of present illness occurred about fifteen years ago, when the knees began to give out. This was followed by a dead feeling in the legs, with inability to walk in the dark. Early fatigue was marked. Severe pains in the legs and around abdomen supervened which were present on admission. Patient had been a sufferer from biliousness for many years.

Examination showed marked bilateral deafness (catarrhal?).

Argyl-Robertson pupils; punched-out scars on shins.

Hypesthesia of the legs; absent knee and Achilles jerks. Ataxic gait; Romberg positive.

Bladder crisis and polyakiuria.

Blood Wassermann negative; luetin positive.

Mere. serum.	Date.	Cerebrospinal fluid.			Wassermann.		Reaction.	Remarks.
		Pressure.	Cells.	Albumin.	C. S. F.	Blood.		
I	July 24	?	5	+	+++	---	Very slight	Bladder, pain still continues.
II	Aug. 8	185	18	+	-	Luetin +	Very slight	Band-like sensations around abdomen. No pain—biliousness.
III	Sept. 5	135	8	-	---	-	No reaction	Weakness. No pain.
IV	Oct. 10	No previous treatment 140	4	-	---	-	No reaction	None.

CASE III.—*Tabes dorsalis*.

W. H., carpenter; aged forty-eight years.

Entered Hospital July 23, 1914, with "rheumatism."

Neisserian infection; 1901, painless sore on penis at same time.

Moderate use of alcohol. Excessive tobacco.

Onset of present illness in 1902, with staggering in the dark.

Marked attacks of nausea and vomiting, with loss in weight and pains in legs.

Examination showed Argyl-Robertson pupils; loss of knee-jerks and ankle-jerks; extreme ataxia and positive Romberg.

Anesthesia of skin of legs and about nipples.

The patient was given two doses of Salvarsan, and mixed treatment, which always disagreed with him.

Fraenkel movements were instituted with good results.

Blood Wassermann + + +.

Mere. serum.	Date.	Cerebrospinal fluid.			Wassermann.		Luetin.	Reaction.
		Pressure.	Cell.	Cell.	C. S. F.	Blood.		
I	Mar. 28	?	31	?	+++	+++	+++	Marked gastric crisis.

Crisis lasted seven days; two small ones since for short time.

Ataxia improved; no pains. Patient had a mild gastric crisis three days one month later.

CASE IV.—*Tabes dorsalis*.

R. W., aged forty-five years, machinist.

Entered hospital December 9, 1914, because of pains in legs and inability to walk.

Gonorrhea and chancre in 1905; no secondaries.

Onset of symptoms, 1907, with numbness in legs followed by staggering at night, especially. Shooting pains in the legs developed. No girdle sensation at first. In the last two years condition became extreme, so that he was taking opiates about 1 grain per day. During this same time patient had four full doses of salvarsan and continuous mercurial treatment.

Examination showed extreme ataxia, positive Romberg; absent knee and Achilles jerks; Argyll-Robertson pupils.

Loss of pain touch and temperature sensibility in legs and abdomen. Hypercraesthesia in the back.

Fraenkel movements were started January 2, 1915, but discontinued because of the pain.

Two doses of neosalvarsan were given on January 7 and 14. Blood Wassermann + + +.

Merc. serum.	Date.	Cerebrospinal fluid.			Wassermann.		Luetin.	Reaction.	Remarks.
		Pressure.	Cells.	Albumin.	C. S. F.	Blood.			
I	Feb. 4	265	40	+	---	+++	+	....	Contamina- tion; hemo- globin.
II	Feb. 18	125	40	+	---	....	...	....	Pupils sluggish; pains disap- peared.
III	Apr. 17	125	3	+	---	....	...	Slight reac- tion	Fraenkel move- ments con- tinued.

Remarks: No pains since second treatment; restraint.

#### CASE V.—*Tabs dorsalis*.

W. M., aged thirty-six years; cabinet-maker.

Entered the hospital April 12, 1915, because of pains in the legs and loss of use of the legs.

Denies lues but admits two Neisserian infections fourteen years ago.

Eight months before admission had soreness and stiffness in legs on walking, so that soon he had little use of his legs. This was accompanied by great shooting pains in the legs and back. Bladder incontinence with dysuria developed.

Examination disclosed Argyll-Robertson pupils; absent knee-jerks and ankle-jerks; disturbed sensation in legs and nipple region.

Marked ataxia and positive Romberg.

Blood Wassermann negative; luetin +.

Cerebrospinal fluid: Wassermann negative.

Mercurial and three salvarsan treatments made no impression on the pains and bladder trouble. The result of treatment by mercurialized serum is shown in the table on page 272.

These cases illustrate in general the results which have been attained. In these 25 selected cases all have improved considerably even when other treatments were totally unavailing.

With improved technic the reaction following the first injection is very slight and consists usually of increase in the pain, slight dull headache, a temperature rising to 99° or 100° and perhaps slight nausea, all of which disappear in eighteen to thirty hours, and are easily controlled by opiates. Subsequent injections cause little or no reaction.

Merc. serum.	Date.	Cerebrospinal fluid.			Wassermann.		Luetin.	Reaction.	Remarks.
		Pressure increased	Cells.	Albumin	C. S. F.	Blood.			
I	May 17	?	100	+	---	---	+	Severe head- aches, temp. 102°. Nau- sea	
II	June 3	?	12	?	---	....	...	Very slight headache and pain in legs. Temp. 98°	Bladder symp- toms im- proved much.
III	June 16	?	17	-	Doubt- ful	....	...	Moderate reaction; pain in legs and hips. Headache. Girdle sen- sation.	Pain disap- peared in twenty-four hours.
IV	Aug. 14	....	25	?	---	....	...	Very slight; 101°; slight headache	Great improve- ment in ataxia.
V	Sept. 10	140	10	-	---	....	...	None	No pain in legs.
VI	Sept. 24	....	8	-	....	....	...	None	Bladder O. K.

Table showing result of treatment by mercurialized serum in Case V.

In the last 100 injections there has been practically no more reaction to the injection beyond that which would occur in any lavage of the subdural space.

Patients originally suffering from gastric crises usually had a severe crisis precipitated by the injections, although there were fewer and less severe crises following in one or two cases. These cases will be studied further. No sphincter disturbances were noted in any case. These are occasionally seen after the Swift-Ellis treatment.

It is important to examine the urine for abnormalities before each treatment, as the presence of albuminuria is, I believe, a distinct contra-indication for treatment.

In 85 Swift-Ellis treatments which I have done there has been no such marked improvement in clinical condition so early, as after the mercurialized serum is given. Occasionally a patient will have a severe outburst of pain, which is of very short duration, in the interval between treatments.

In the first case mentioned the bladder disturbance entirely cleared up after the second injection. The cellular contents of the spinal fluid rapidly diminished with the treatment in cases in which an abnormal count was found.

CONCLUSIONS. The facts of greatest interest to the neurologist in connection with the intraspinal mercurialized serum treatment are:

1. There is no danger in its administration.
2. For local treatment it is very efficacious in syphilis of the central nervous system, especially in the treatment of tabes dorsalis, in which lancinating pains are the predominant symptom.
3. Due to its stability the serum may be used at any time after its preparation.



4. The lack of expensive drugs used in its preparation makes it invaluable at this time.

5. There is no objection to a combined salvarsanized and mercurialized treatment.

6. It must not be concluded from the short space of time (eight months) that has elapsed since the beginning of this form of treatment in these cases that relief is going to be permanent. One will have to be cautious about prognosticating a cure until the proper length of time elapses, *e. g.*, at least three years. From the results obtained so far it certainly has mitigated the symptom of pain.

### HEMATEMESIS DUE TO CHRONIC APPENDICITIS, WITH AN EXPLANATION OF ITS PATHOLOGICAL PHYSIOLOGY.

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THE patient was a male, aged fifty years, by occupation a farmer. He was always well up to ten years before operation, although he has always been severely constipated. This began to be progressively worse at this period. He never had a definite attack of colic or acute abdominal illness.

Five years and a half before the operation he consulted a competent gastrologist, whose records we have been privileged to examine. The principal complaint was constipation and sour stomach, with eructations of acid material. Vomiting was not present to any extent. There was pain in the epigastrium before and after meals. He had never vomited blood except a few times after prolonged hiccoughing spells, which he often had. An examination of the stomach contents at this time discovered hyperacidity and hypersecretion. He was treated for a time, and was well after going home for about a year, when the same symptoms returned. He was treated by various methods with only temporary relief for about four years, when he presented himself for operation, advised by the gastrologist who had formerly examined him.

He had lost a few pounds in weight. The prominent symptom was still epigastric pain and recurrent vomiting. Two weeks before he had vomited twice, bringing up a pint of dark red blood each time. He was not jaundiced. There was considerable rigidity along the right rectus muscle and tenderness over the epigastrium, under the right ribs and in the right iliac fossa. He was given a test meal. He